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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,070	TRUNE, DENNIS R.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant has cancelled claim 27. Applicant elected Group I claims 1-26 in the response filed on 6/26/07. Applicant has not stated "with" or "without" traverse, and thus because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites "a mimetic or analog". It is unclear to the Examiner what might be a mimetic or analog of fludrocortisone. An example of fludrocortisone acetate is provided as an analog of fludrocortisone on page 4, lines 9-14 of the instant specification, but this single chemical enitity does not provide a clear structure to all the possible analogs that might exist. Claims 2-26 are rejected as being indefinite because they are dependent on an indefinite base claim. The Examiner will examine the claims as they read on fludrocortisone.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10, 12-15, 17-19, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Henkin et al. The Journal of Clinical Investigation 1968, 47, 1269-1280.

Henkin et al. disclose tested the auditory perception of patients with Addison's Disease (autoimmune adrenalitis) as compared to normal volunteers and report that steroid replacement therapy results in restoration of detection sensitivity and perceptual ability (Abstract, page 1269). Henkin et al. disclose a treatment where the patients were treated with dosages of 9 alpha-fluorohydrocortisone, which is fludrocortisone, (0.05-0.10 mg/day) and prednisolone (5.0-7.5 mg/day) (page 1270, Methods). In the absence of evidence to the contrary, the patients had hearing loss in both ears. Since the active agent is the same as instantly claimed then administration of the composition would decrease sodium-potassium imbalances in an endolymph of a stria vascularis of the subject and would increase sodium transport in a stria vascularis. Since the limitations of instant claim 1 have been met then it is the Examiner's position that the sodium transport would be increased by at least 10% in the absence of evidence to the contrary. It is the Examiner's position that administration of the fludrocortisone would inherently increase sodium and potassium transport in a stria vascularis. Prednisone is a glucocorticoid that is co-administered and thus reads on instant claims 17-19. Since the limitations of instant claim 1 have been met then it is the Examiner's position that the hearing would be increased by at least 10% and by at least 20% prior to

administration of the composition in the absence of evidence to the contrary and thus anticipate instant claims 24 and 25.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henkin et al. The Journal of Clinical Investigation 1968, 47, 1269-1280 in view of Lamm et al. (Otorhinolaryngol Nova 1999, 9, 203-216),with respect to claims 2, 4, 5, 7-9, 16 and 21-23, and Okamura et al. Abstract (Auris Nasus Larynx 1992, 19(1), 1-6) and Caldarelli et al. Abstract (Am J Otol. 1986, 7(3) 210-213) with respect to claim 3.

Applicant claims a method for treating sensorineural cochlear hearing loss in a subject comprising administering a composition comprising fludrocortisone.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The reference of Henkin et al. is described in detail above and that discussion is hereby incorporated by reference.

Lamm et al. teach corticosteroid treatment in cochlear disorders such as Meniere's disease and idiopathic acute sensorineural hearing loss (title; abstract). Lamm et al. teaches that fludrocortisone exerts a 10-fold anti-inflammatory and 125-fold sodium retaining potency (page 205, synthetic analogs of glucocorticoids). Lamm et al. teach transtympanic injection of the glucocorticoids as well as systemic administration (page 208, glucocorticoids applied locally onto the round window membrane and systemically applied glucocorticoids).

Okamura et al. teach hearing loss in Wegener's granulomatosis can be improved by administration of steroids (Abstract).

Caldarelli et al. teach sensorineural hearing loss in a patient with lupus erythematosus and treatment with prednisone (Abstract).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. While Applicant claims wherein the autoimmune disease is Wegener's granulomatosis, polyarteritis nodosa or systemic lupus erythematosus, Henkin et al. do not expressly teach these automimmune diseases. This deficiency in Henkin et al. is cured by the teachings of Okamura et al and Caldarelli et al.

2. While Applicant claims wherein the subject has sudden or idiophathic hearing loss, Henkin et al. do not expressly teach sudden or idiopathic hearing loss. This deficiency in Henkin et al. is cured by the teachings of Lamm et al.

3. While Applicant claims wherein the subject has endolymphatic hydrops or Meniere's disease, Henkin et al. do not expressly teach endolymphatic hydrops or Meniere's disease. This deficiency in Henkin et al. is cured by the teachings of Lamm et al.

4.While Applicant claims wherein the fludrocortisone is fludrocortisone acetate, Henkin et al. do not expressly teach wherein the fludrocortisone is fludrocortisone acetate.

5. While Applicant claims wherein the hearing loss is a reduction in hearing by at least 20%; or at least 50%; and in one ear, Henkin et al. do not expressly teach wherein the hearing loss is a reduction in hearing by at least 20%; or at least 50%; and in one ear.

6. While Applicant claims wherein the composition comprises a pharmaceutically acceptable carrier; administered orally; administered to the middle ear; administered transtympanically, Henkin et al. do not expressly teach wherein the composition comprises a pharmaceutically acceptable carrier; administered orally; administered to the middle ear; administered transtympanically. This deficiency in Henkin et al. is cured by the teachings of Lamm et al.

7. While Applicant claims wherein the prednisone is administered at a dose of about 60-800 ug/kg/day and the fludrocortisone is administered at a dose of about 100-

200 ug/kg/day, Henkin et al. do not expressly teach wherein the prednisone is administered at a dose of about 60-800 ug/kg/day and the fludrocortisone is administered at a dose of about 100-200 ug/kg/day.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Henkin et al. wherein the autoimmune disease is Wegner's granulomatosis or lupus erythematosus, as suggested by Okamura et al. and Caldarelli et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Okamura et al. teach that steroids improve hearing loss in subjects suffering from Wegener's granulomatosis and Henkin et al. teach that steroids, such as fludrocortisone, bring hearing back to normal (abstract of Henkin et al.). In addition Caldarelli et al. report that prednisone did not improve hearing loss such that one of ordinary skill in the art would look for better treatment options such as fludrocortisone.

2 and 3. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Henkin et al. wherein the subject has sudden or idiophathic hearing loss or Meniere's disease, as taught by Lamm et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Lamm et al. teach these forms of hearing loss and treatment with corticosteroids.

4. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Henkin et al. wherein the fludrocortisone is fludrocortisone acetate and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because fludrocortisone acetate is rendered obvious by fludrocortisone taught by Henkin et al.

5. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Henkin et al. wherein the hearing loss is a reduction in hearing by at least 20%; or at least 50%; and in one ear and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Henkin et al. teach treating patients with decreased auditory ranges and treatment with the steroids returned auditory detection and perception to normal. Determination of the reduction in hearing and which ear, is merely a matter of routine testing by one of ordinary skill in the art.

6. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Henkin et al. wherein the composition comprises a pharmaceutically acceptable carrier; administered orally; administered to the middle ear; administered transtympanically, as suggested by Lamm et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because composition formulations for oral or intravenous administration are readily known to one of ordinary skill in the art and it is merely routine optimization to suit the best mode of

administration and Lamm et al. teach transtympanic injections as one possible mode of administration.

7. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Henkin et al. wherein the prednisone is administered at a dose of about 60-800 ug/kg/day and the fludrocortisone is administered at a dose of about 100-200 ug/kg/day and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because it is merely routine optimization of the dosages provided by Henkin et al. to arrive at the instantly claimed ranges.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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